

DRUG CHART

PSYCHOACTIVE DRUGS: Substances that have their effect on the nervous system, mind or psyche. These drugs change how you feel. They change your sense of well being.

	IMMEDIATE EFFECTS	TOXIC EFFECTS (OVERDOSE)	LONG TERM PROBLEMS	MEDICAL USES	TYPE OF HIGH
ALCOHOL (BEER, WINE, DISTILLED SPIRITS)	Low dose: Giddy - relax High dose: Slowed reflexes Slurred speech Decreased mental activity ACCIDENTS	Hang over Stomach upset Pass out	Alcoholic syndrome Drunk Driving	?Relaxation? ?slow labor?	Mild Euphoria Relaxation Sleepy high
MARIJUANA	Eye congestion increase desire for food time-space distortion light headedness	Paranoia and Hallucinations	Amotivational syndrome Cellular damage CHRONIC LUNG DISEASE	?Adjunct to cancer therapy? ?glaucoma? (No longer being studied by the FDA)	Dreamy euphoric state
STIMULANTS					
Amphetamine	Alertness Appetite suppression Enhanced sense of capacity	Psychosis Hyperactivity Cardiac arrhythmias	Sleep disruption Psychosis	Hyperactivity in Children (rarely)	Stimulation
Cocaine	Alertness Intense euphoria	Psychosis Death HEART SEIZURES	Psychosis Drug seeking behavior	Local anesthetic	"Orgasmic" type of stimulation
RITALIN (?)	<i>MILD STIMULATION</i>		<i>DEPENDENCE</i>	<i>ADHD</i>	<i>MILD</i>
OPIATES (NARCOTICS)	<i>(RELIEVE PAIN and PRODUCE SLEEP)</i>				
Morphine	"feel good" euphoria DROWSINESS	Depressed respiration Lung congestion and convulsions	Addiction	Pain relief	"feel good" Euphoria
Methadon	Less euphoria than morphine	Safer than morphine	Addiction	Treatment for heroin addicts	milder than morphine
Heroin	Intense "feel good" euphoria	Depressed respiration Lung congestion and CONVULSIONS	Strong physical addiction Drug seeking behavior	none	Intense "feel good" euphoria
Opium			Addiction	none	
Codeine	Mild buzz		Addiction	Pain relief Cough suppression	<i>MILD BUZZ</i>
OXYCODONE	<i>TRADE NAME OXYCONTIN</i>			<i>TIME RELEASE PAIN RELIEF</i>	

	IMMEDIATE EFFECTS	TOXIC EFFECTS (OVERDOSE)	LONG TERM PROBLEMS	MEDICAL USES	TYPE OF HIGH
BARBITURATES (SEDATIVES AND HYPNOTICS)					
Quaalude	Relaxation	Confusion	Physical addiction	Insomnia	Sleepy high
Phenobarbital	"sleepy" high	Poor coordination	Hide the real problem	Anxiety	Relaxation
Secobarbital	Decreased mental activity	Depression		Epilepsy	
Amobarbital		Convulsions		Anesthesia	
Pentobarbital		coma			
GHB - GAMMA HYDROXY BUTYRATE					

TRANQUILIZERS-ANTI ANXIETY-ANTICONVULSANTS-ANTIDEPRESSANTS-ETC.					
Valium	Tranquil feeling	Depression	Psychological dependence	Mood disorders	Nothing bothers you
Thorazine	Euphoric, sleepy high		Hide the real problem	Depression	"tranquil"
Prozac				Mania	Sleepy high
Librium				Neuroses	
Xanax	(There are many (at least 73) drugs in this group. These drugs are not very dangerous but should not be used without a doctors advice.)			Psychoses	
ROHYPNOL					

HALLUCINOGENS

LSD	Hallucinations	Psychosis Flash backs Anxiety or panic	Psychosis	none	Hallucination Good trips Bad trips
Mescaline	Hallucinations	Psy, FB, Anx or Panic	Psychosis	none	Hallucination
Peyote cactus					Good-bad
Psilocybin mushrooms	Hallucinations	Psy, FB, Anx, or Panic	Psychosis	none	Hallucination Good-bad
Phencyclidine	Hallucinations	Convulsions & Psychosis	Chronic brain Syndrome	none	Hallucination & euphoria
MDMA - ECSTASY - HALLUCINATIONS + STIMULATION					
KETAMINE - SPECIAL K					

more bad than good

INHALANTS

Nitrous Oxide (laughing gas)	disorientation		BIRTH DEFECTS IF PREGNANT	Dental Pain	?
Amyl Nitrate	Nausea	Unconsciousness	Hepatitis	none (no longer used For heart medication)	?
Butyl Nitrate		Death	Brain damage	none	
		Violent behavior	Nervous system damage	none	?
Chlorohydrocarbons (Aerosol cans)				none	?
Hydrocarbons (Aerosol cans, gasoline, glue, paint thinner)				none	?

DESIGNER DRUGS: Drugs in some of the above categories can be changed to give more intense highs, quicker action, and stronger effects. They also produce more powerful addictions and toxic effects.

OTHER DRUGS: Anabolic steroids, nicotine.

TERMS: Drug, pharmacology, drug effects, medical effects, side effects, therapeutic dose, toxic dose, physical dependence, psychological dependence, drug addiction, withdrawal, tolerance, drug administration, placebo, trade name, generic name, FDA, OTC, prescription, double blind condition, synergistic effect.

In 1994, the Harvard School of Public Health, with support from the Robert Wood Johnson Foundation, published a study of binge drinking on 140 college campuses nationwide. A total of 17,592 students participated. High binge-drinking schools were identified as large public colleges in the Northeast or the

Midwest with a bar within a one-mile radius, boasting strong athletic programs, having residence halls on campus and allowing twenty-one-year-olds to drink there, maintaining an active fraternity and sorority system, and serving alcohol on campus. Though not named in the study, Penn State was one of the participating schools and received results particular to its undergraduate population. According to the study:

- 62 percent of Penn State students binged when they drank
- 47 percent were drunk three or more times in the past month
- 72 percent experienced hangovers because of drinking
- 46 percent missed a class
- 44 percent did something they regretted
- 45 percent forgot where they were or what they did
- 26 percent participated in unplanned sexual activity
- 51 percent drink to get drunk
- 37 percent had been insulted or humiliated by someone who was drinking
- 60 percent had to “baby-sit” a drunken student
- 30 percent experienced unwanted sexual advances
- 0 percent considered themselves a problem drinker

Beer as health food

PERHAPS LIKE many sensible citizens, you read Investor's Business Daily for its sturdy common sense in defending free markets and other rational arrangements.



GEORGE
WILL

If so, you, too, may have been startled recently by an astonishing statement on that newspaper's front page. It was in a report on the intention of the world's second-largest brewer, Belgium's In-Bev, to buy control of the third-largest, Anheuser-Busch, for \$46.3 billion. The story asserted: "The [alcoholic beverage] industry's continued growth, however slight, has been a surprise to those who figured that when the economy turned south, consumers would cut back on non-essential items like beer. ..."

"Non *what*"? Do not try to peddle that proposition in the bleachers or at the beaches in July. It is closer to the truth to say: No beer, no civilization.

The development of civilization depended on urbanization, which depended on beer. To understand why, consult Steven Johnson's marvelous 2006 book, "The Ghost Map: The Story of London's Most Terrifying Epidemic – and How It Changed Science, Cities, and the Modern World." It is a great scientific detective story about how a horrifying cholera outbreak was traced to a particular neighborhood pump for drinking water. And Johnson begins a mind-opening excursion into a related topic this way:

Lifesaver

"The search for unpolluted drinking water is as old as civilization itself. As soon as there were mass human settlements, waterborne diseases like dysentery became a crucial population bottleneck. For much of human history, the solution to this chronic public-health issue was not purifying the water supply. The solution was to drink alcohol."

The development of civilization depended on urbanization, which depended on beer.

Often the most pure fluid available was alcohol -- in beer and, later, wine -- which has antibacterial properties. Sure, alcohol has its hazards, but as Johnson breezily observes, "Dying of cirrhosis of the liver in your forties was better than dying of dysentery in your twenties." Besides, alcohol, although it is a poison, and an addictive one, became, especially in beer, a driver of a species-strengthening selection process.

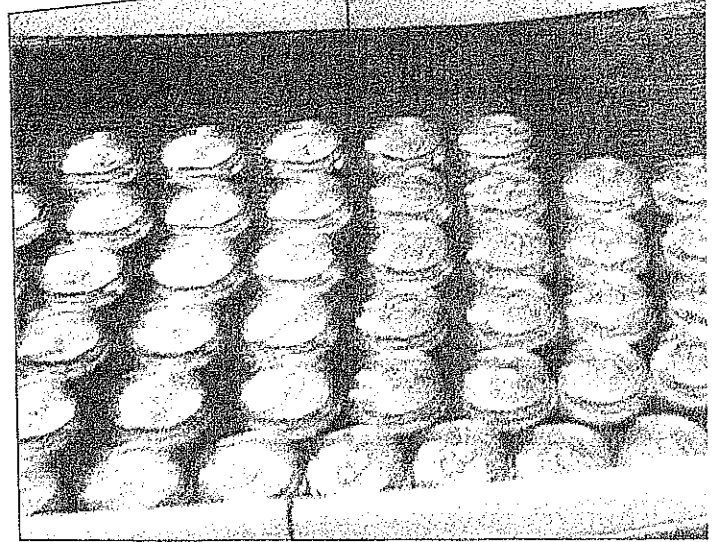
Johnson notes that historians interested in genetics believe that the roughly simultaneous emergence of urban living and the manufacturing of alcohol set the stage for a survival-of-the-fittest sorting-out among the people who abandoned the hunter-gatherer lifestyle and, literally and figuratively speaking, went to town.

To avoid dangerous water, people had to drink large quantities of, say, beer. But to digest that beer, individuals needed a genetic advantage that not everyone had -- what Johnson describes as the body's ability to respond to the intake of alcohol by increasing the production of particular enzymes called alcohol dehydrogenases. This ability is controlled by certain genes on chromosome four in hu-

man DNA, genes not evenly distributed to everyone. Those who lacked this trait could not, as the saying is, "hold their liquor." So, many died early and childless, either of alcohol's toxicity or from waterborne diseases.

The gene pools of human settlements became progressively dominated by the survivors -- by those genetically disposed to, well, drink beer. "Most of the world's population today," Johnson writes, "is made up of descendants of those early beer drinkers, and we have largely inherited their genetic tolerance for alcohol."

Johnson suggests,



not unreasonably, that this explains why certain of the world's population groups, such as Native Americans and Australian Aborigines, have had disproportionately high levels of alcoholism: These groups never endured the cruel culling of the genetically unfortunate that town dwellers endured. If so, the high alcoholism rates among Native Americans are not, or at least not entirely, ascribable to the humiliations and deprivations of the reservation system. Rather, the explanation is that not



enough of their ancestors lived in towns.

Good news

But that is a potential stew of racial or ethnic sensitivities that we need not stir in this correction of Investor's Business Daily. Suffice it to say that the good news is really good: Beer is a health food. And you do not need to buy it from those wan, unhealthy-looking people who, peering disapprovingly at you through rimless Trotsky-style spectacles, seem to run all the health food stores.

So let there be no more loose talk — especially not now, well into summer — about beer not being essential. Benjamin Franklin was, as usual, on to something when he said, "Beer is living proof that God loves us and wants us to be happy." Or, less judgmentally, and for secular people who favor a wall of separation between church and tavern, beer is evidence that nature wants us to be.

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ESSAY

Addiction Doesn't Discriminate? Wrong

By SALLY SATEL, M.D.

We've heard it before. "Drug abuse is an equal opportunity destroyer." "Drug addiction is a bipartisan illness." "Addiction does not discriminate; it doesn't care if you are rich or poor, famous or unknown, a man or woman, or even a child."

The phrase "addiction doesn't care" is not meant to remind us that addiction casts a long shadow — everyone knows that. Rather, it is supposed to suggest that any individual, no matter who, is vulnerable to the ravages of drugs and alcohol.

The same rhetoric has been applied to other problems, including child abuse, domestic violence, alcoholism — even suicide. Don't stigmatize the afflicted, it cautions; you could be next. Be kind, don't judge.

The democratization of addiction may be an appealing message, but it does not reflect reality. Teenagers with drug problems are not like those who never develop them. Adults whose problems persist for decades manifest different traits from those who get clean.

So while anyone can theoretically become an addict, it is more likely the fate of some, among them women sexually abused as children; truant and aggressive young men; children of addicts; people with diagnosed depression and bipolar illness; and groups including American Indians and poor people.

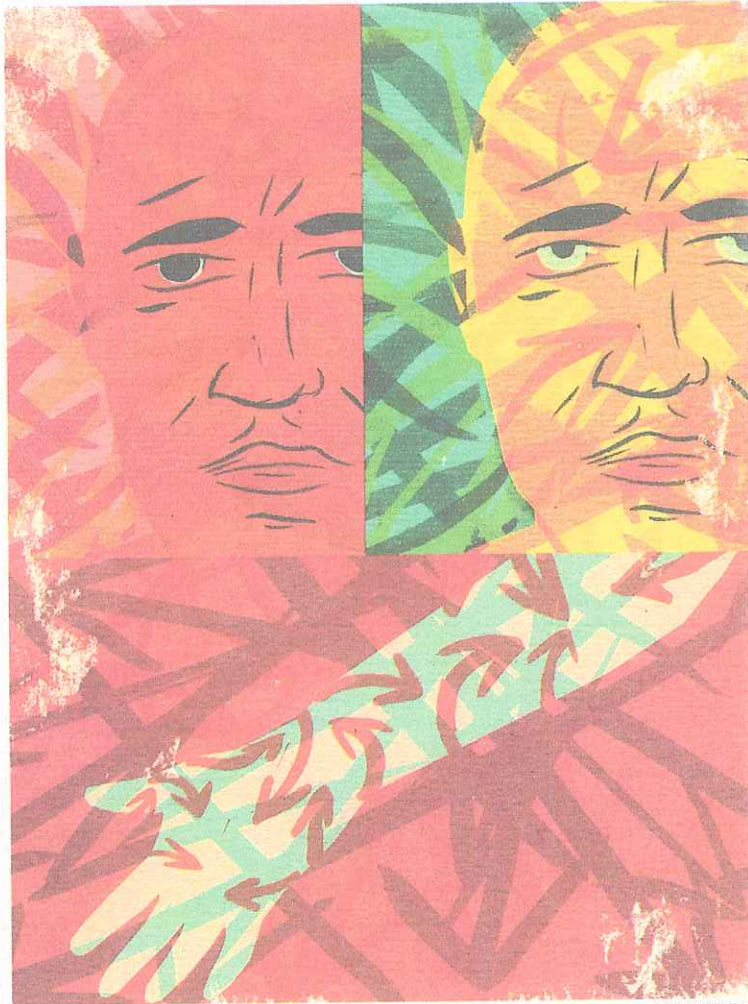
Attitudes, values and behaviors play a potent role as well.

Imagine two people trying cocaine, just to see what it is like. Both are 32-year-old men with jobs and families. One snorts a line, loves it and asks for more. The other also loves it but pushes it away, leaves the party and never touches it again. Different values? Different tolerance for risk? Many factors may distinguish the two cocaine lovers, but only one is at risk for a problem.

Asking for more drug is no guarantee of being seduced into routine use. But what if it happens? Jacob Sullum, a senior editor at Reason magazine, has interviewed many users who became aware that they were sliding down the path to addiction. "It undermined their sense of themselves as individuals in control of their own destinies," Mr. Sullum wrote in his 2003 book, "Saying Yes: In Defense of Drug Use." "And so they stopped."

I only read about these people. Patients who come to our methadone clinic are there, obviously, because they're using. The typical patient is someone who has been off heroin for a while (I say because life was good for

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EDWARD MCGOWAN

Slogans aside, addiction is a more likely fate for some.

while, maybe because there was no access to drugs, maybe because the boss did urine testing) and then resumed.

But the road to resumption was not unmarked. There were signs and exit ramps all along the way. Instead of heeding them, our patients made small, deliberate choices many times a day — to be with other users, to cop drugs for friends, to allow themselves to become bored — and soon there was no turning back.

Addiction does indeed discriminate. It "selects" for people who are bad at delaying gratification and gauging consequences, who are impulsive, who think they have little to lose, have few

competing interests, or are willing to lie to a spouse.

Though the National Institute on Drug Abuse describes addiction as a "chronic and relapsing disease," my patients, seeking help, are actually the exception. Addiction is not an equal opportunity destroyer even among addicts because, thankfully, most eventually extricate themselves from the worst of it.

Gene Heyman, a lecturer and research psychologist at Harvard Medical School and McLean Hospital, said in an interview that "between 60 and 80 percent of people who meet criteria for addiction in their teens and 20s are no longer heavy, problem users by their 30s." His analysis of large national surveys revealed that those who kept using were almost twice as likely to have a concurrent psychiatric illness.

None of this is to deny that brain physiology plays a meaningful role in becoming and stay-

ing addicted, but that is not the whole story.

"The culture of drink endures because it offers so many rewards: confidence for the shy, clarity for the uncertain, solace to the wounded and lonely," wrote Pete Hamill in his memoir, "A Drinking Life." Heroin and speed helped the screenwriter Jerry Stahl, author of "Permanent Midnight," attain the "the soothing hiss of oblivion."

If addiction were a random event, there would be no logic to it, no desperate reason to keep going back to the bottle or needle, no reason to avoid treatment.

The idea that addiction doesn't discriminate may be a useful story line for the public — if we are all under threat then we all should urge our politicians to support more research and treatment for addiction. There are, good reasons to campaign for those things, but not on the basis of a comforting fiction.

Fear of Opioid Addiction Means Untreated Pain

MEDIA coverage of OxyContin abuse has ignited long-standing fears about opioids, a group of pain-relieving drugs related to opium. As many as 300 fatal OxyContin overdoses may have occurred in the last 2 years; the medication can provide an immediate high when crushed because the entire dose of its active ingredient, a synthetic form of morphine known as oxycodone, is released at once.

As a result of the negative publicity, medically appropriate use of opioids to treat pain has been overshadowed by misperceptions that all opioids are dangerous drugs. Many people—despite severe pain—do not want to take them, fearing addiction as well as social stigma.

Patients are not always alone in harboring concerns over opioids. Many physicians are also wary. Daniel Carr, MD, medical director of the Tufts-New England Medical Center's Pain Management Program, says that while there's a growing acceptance of opioids in the medical community, "doctors are members of society too, so they share some of the same fears of the drugs."

For instance, opioids are the mainstay for the mitigation of cancer pain as well as short-term pain resulting from, say, an injury or surgery, but increased wariness of them is leading to their being underprescribed. Physicians are even more hesitant to prescribe them for people with long-term pain unrelated to cancer, such as back pain. Such underutilization of opioids means that many Americans with chronic pain are suffering needlessly.

The truth about opioid addiction

Opioids act by binding to receptors in the brain and spinal cord. In doing so, they blunt the transmission of pain messages to the brain. Some opioids, like morphine and codeine, are naturally derived from opium, while others, including methadone and fentanyl, are synthetic.

Both types carry the potential for addiction and abuse. But "addiction is an unlikely event" in people who take opioids for chronic pain under a physician's careful supervision, says Tufts's Dr. Carr. Indeed, when investigators at the University of Wisconsin Medical School compared national data on medical use and abuse of five opioid painkillers over a 6-year period, they found that despite a significant increase in prescriptions, there were not significantly more cases of opioid abuse.

The fear of opioid addiction in the face of evidence to the contrary is based largely on people's confusion about what addiction actually means. **Many people erroneously equate addiction with physical dependence. People who take opioids for a prolonged period of time usually do develop physical dependence**, which means that they would experience withdrawal symptoms—nausea, vomiting, cramps, tremors—if the medication were abruptly discontinued.

But this is a normal state of adaptation that can occur with drugs other than opioids and that can be prevented by gradually tapering the dosage.

Addiction, by contrast, is an adverse response to a medication with a strong psychological component, characterized by craving and compulsively seeking the drug. Someone who is addicted is preoccupied with obtaining and using the substance to such an extent that his or her day-to-day function becomes greatly impaired. **People who are addicted to opioids often exhibit "drug-seeking" behaviors, such as visiting multiple doctors and "losing" prescriptions.**

According to June Dahl, PhD, professor of pharmacology at the University of Wisconsin Medical School and co-author of the 6-year study on opioid abuse, the few people who do become addicted to medically prescribed opioids and exhibit those behaviors generally have a prior history of substance abuse. Furthermore, researchers speculate that people who seek drugs for illicit rather than medicinal purposes have a genetic predisposition to addiction. Many develop a tolerance to the drugs, too, needing more and more to feel the same effects, while most people *prescribed* opioids are able to stay at a constant dose of medication for a long period of time without a reduction in the drug's pain-killing effects. In other words, it's not the opioid that's the source of the trouble as much as the opioid taker. Opioids are not "intrinsically dangerous," comments Russell Portenoy, MD, chairman of the Department of Pain Medicine and Palliative Care at Beth Israel Hospital in New York.

A protocol for including opioids in pain treatment

To allay concerns about opioids, the Federation of State Medical Boards, which is the umbrella organization for all the medical boards across the country, issued guidelines a few years ago on prescribing opioids for the treatment of chronic pain while minimizing the risk for addiction and abuse. "Physicians have been overly cautious [in prescribing opioids] because they are worried about addicting patients and regulatory action," says Dr. Dahl. "But if you practice good medicine, meaning you develop a treatment plan, conduct periodic evaluation of the response to treatment, and document the results, you won't get in trouble."

So far, the majority of research conducted on the long-term success of opioid therapy has been limited to cancer pain. However, as the role of opioids in the treatment of non-cancer pain gains acceptance, pain experts believe there will be a corresponding growth in studies that will bolster what they are seeing firsthand—that many people with chronic pain truly benefit from opioids, achieving a greater level of function and an improved quality of life. "The body of anecdotal evidence [for opioids' benefits] is very large," says Dr. Portenoy. "They are not a panacea, but they're effective."

Did you know... People with diabetes are two to four times more likely than others to have cardiovascular trouble such as a heart condition or stroke.

For Chronic Fatigue, Placebos Fail the Test

By NICHOLAS BAKALAR

Many doctors believe that sugar pills are likely to be effective for patients with chronic fatigue syndrome, trusting that a placebo will help relieve the mental and physical exhaustion that characterize the illness.

But a new study has found that people who have the syndrome respond at a lower rate to placebos than patients with other diseases. The paper was published in the March-April issue of *Psychosomatic Medicine*.

Studies suggest that placebos relieve the symptoms for about 30 percent of patients suffering from a wide variety of illnesses. Migraine headaches, for example, respond at a rate of about 29 percent to placebo treatment, major depression at about 30 percent and reflux esophagitis at about 26 percent.

In some diseases, placebo treatments are even more effective — 36 to 44 percent of patients with duodenal ulcers improve on placebos, depending on how many of the treatments are offered each day.

But by pooling results from more than two dozen studies, the researchers, led by Dr. Hyong Jin Cho, a professor of psychiatry at King's College London, found that, among people with chronic fatigue syndrome, only 19.6 percent responded to placebos, not the 50 percent found by previous, less systematic studies.

To Dr. Cho, the results were both unexpected and disappointing: he says he believes placebos can be a legitimate and useful form of medical treatment. He concluded not that placebos were unhelpful in treating chronic fatigue but that their use should be perfected.

"At the clinical practice level," he wrote, "the overall low placebo response emphasizes the need to enhance" the placebo effect in treating the illness.

To many doctors, chronic fatigue syndrome seems like a perfect candidate for placebo treatment, Dr. Cho and his colleagues write. Its symptoms are often indistinct: in addition to general fatigue, patients complain of muscle and joint pain, headaches, memory impairment and mood disturbances. Moreover, the symptoms frequently fluctuate over time, and they are more acute when the patients are paying close attention to them.

The illness has no cure, and the Centers for Disease Control and Prevention estimates that as many as 500,000 Americans suffer from it.

Dr. Cho and his colleagues speculate that the skepticism about the illness on the part of health care professionals may damage the trust between doctor and patient — a factor that may influence the effect of a placebo.

According to the study, placebos presented as medical or alternative-complementary treatments have a greater effect with chronic fatigue patients than do those offered as psychiatric interventions. The researchers suggest that this may be because most patients have a firm prior belief that the illness is physical. They make no judgment about the accuracy of that belief.

But Dr. Brian Fallon, an associate professor of psychiatry at Columbia University, offers a different interpretation. The fact that chronic fatigue syndrome responds so poorly to placebo treatment, he said, provides evidence that the

Can a sugar pill trick your symptoms?

syndrome has a physiological basis, though one that is still poorly understood.

"The finding by Dr. Cho and colleagues will come as no surprise to patients with C.F.S. who experience debilitating fatigue despite numerous treatment interventions," Dr. Fallon said. "That the placebo response in C.F.S. was far lower than in primary psychiatric disorders such as depression highlights the distinct nature of C.F.S. and how little we know."

Whatever conclusions may be drawn from the study's results, Dr. Cho says he sees placebo treatments as important.

"Many alternative therapies may provide a cure that depends on this powerful placebo effect," he said in an e-mail message. "I'm not using the term pejoratively, since empathy and time spent with the patient by the professionals in this area are indeed of important therapeutic value."

Placebo Effect Is More Myth Than Science, Study Says

By GINA KOLATA

In a new report that is being met with a mixture of astonishment and sometimes disbelief, two Danish researchers say the placebo effect is a myth.

The investigators analyzed 114 published studies involving about 7,500 patients with 40 different conditions. The report found no support for the common notion that, in general, about a third of patients will improve if they are given a dummy pill and told it is real.

Instead, the researchers theorize, patients seem to improve after taking placebos because most diseases have uneven courses in which their severity waxes and wanes. In studies in which treatments are compared not just with placebos but also with no treatment at all, they said, participants given no treatment improve at about the same rate as participants given placebos.

The paper appears today in the New England Journal of Medicine. Both authors, Dr. Asbjorn Hrobjartsson and Dr. Peter C. Gotzsche, are with the University of Copenhagen and the Nordic Cochran Center, an international organization of medical researchers who review randomized clinical trials.

Dr. Hrobjartsson said he had been telling other investigators what he found and watching their responses.

"People react with surprise, but also with a kind of satisfaction," he said in a telephone interview. "They start reflecting."

Experts interviewed this week had a range of responses from ready acceptance of the conclusion to great surprise to a skepticism and the desire to see the details of the analysis.

Dr. Donald Berry, for example, a statistician at the M. D. Anderson Cancer Center in Houston, said: "I believe it. In fact, I have long believed that the placebo effect is nothing more than a regression effect," referring to a well-known statistical observation that a patient who feels particularly terrible one day will almost invariably feel better the next day, no matter what is done for him.

Another physician, Dr. Jonathan Moreno, director of the Center for the Biomedical Ethics at the University of Virginia, said it rang

true to him. "Maybe it is one of the urban legends of medicine," he said.

But others, like David Freedman, a statistician at the University of California, said he was not convinced. Professor Freedman said the statistical method the Danish researchers used, pooling data from many studies and using a statistical tool called metanalysis to examine them, could give misleading results.

"I just don't find this report to be incredibly persuasive," he said. "The evidence of a placebo effect is maybe a little bit less than I thought it was, but I think there's a big effect in many circumstances. This doesn't change my mind."

The researchers said they saw a slight effect of placebos on subjective outcomes reported by pa-

Finding what may simply be a disease's natural course.

tients, like their descriptions of how much pain they experienced. But, Dr. Hrobjartsson said, he questions that effect.

"It could be a true effect, but it also could be a reporting bias," he said. "The patient wants to please the investigator and tells the investigator, 'I feel slightly better.'"

Placebos are still needed in clinical research, Dr. Hrobjartsson said, to prevent researchers from knowing who is getting a real treatment. Otherwise, he said, researchers can end up seeing what they want to see. For example, they may notice changes in patients who are taking an active drug while not paying as much attention to similar symptoms in patients that they know are being left untreated. Patients, he said, who are told they are not being treated may leave the study, further complicating research efforts.

Dr. Hrobjartsson and Dr. Gotzsche said they began their study out of curiosity. Over and over, medical journals and text-

books asserted that placebo effects were so powerful that, on average, 35 percent of patients would improve simply if they were told that a dummy treatment was real. The investigators began asking where this assessment came from. Every paper, Dr. Hrobjartsson said, seemed to refer to other papers. And those papers referred him to other papers. He began peeling back the onion, finally coming to the original paper. It was written by a Boston doctor, Henry Beecher, who had been chief of anesthesiology at Massachusetts General Hospital in Boston and in 1955 published a paper, "The Powerful Placebo" in The Journal of the American Medical Association.

In his paper, Dr. Beecher, who died in 1976, reviewed about a dozen studies that compared placebos with active treatments and concluded that placebos had medical effects.

"He came up with the magical 35 percent number that has entered placebo mythology," Dr. Hrobjartsson said.

But, Dr. Hrobjartsson said, diseases naturally wax and wane. And no matter how sick the person is, a truly bad spell will almost inevitably be followed by a period in which the condition seems to improve. What if the natural variation in a disease's course is behind the placebo effect, they asked?

"Of the many articles I looked through, no article distinguished between a placebo effect and the natural course of a disease," Dr. Hrobjartsson said. "This is a very banal error to make, but sometimes banal errors are made."

He and Dr. Gotzsche began looking for well-conducted studies that divided patients into three groups, giving one a real medical treatment, one a placebo and one nothing at all. That was the only way, they reasoned, to decide whether placebos had any medical effect.

But they worried that there might be so few such studies with a treated, untreated and placebo group that they would never be able to answer the question. "We thought if we could find 20, that would be a huge success," Dr. Hrobjartsson said.

To their surprise, they found 114, published between 1946 and 1998. The conditions included from med-

Among some scientists, a belief that a report is unconvincing.

ical disorders, like high blood pressure, high cholesterol levels and asthma; behavioral disorders and addictions, like alcohol abuse and smoking; neurological diseases like Alzheimer's disease, Parkinson's disease, and epilepsy, and infections, like bacterial infections and the common cold.

When they analyzed the data, they could detect no effects of placebos on objective measurements, like cholesterol levels or blood pressure.

Dr. John C. Bailar III, an emeritus professor at the University of Chicago who wrote an editorial accompanying the placebo paper, said the findings called into question some mind-body beliefs. These are arguments that use the placebo effect to conclude that the mind can so profoundly affect the course of a disease that people should be able to harness this power and think themselves well.

The findings should also give doctors pause in prescribing treatments they know are useless, like a glass of warm milk at bedtime for patients with insomnia or futile drugs for patients in the late stages of fatal diseases, Dr. Bailar said.

"I think what this ought to do is bring about a very sharp reduction in the use of placebos," he said. "My guess is that it will bring about a modest reduction and that it will take a second or third penetrating paper to bring about a real change."

But, Dr. Bailar said, he understands the reluctance many will feel to abandon their belief in placebos. He, too, is hesitant to wrench himself completely away from what he now thinks is largely a myth.

"I'm not ready to give up on placebos entirely," Dr. Bailar said. "I hope there will be a lot more research on how they work."

Or, he said, "if they work."

The New York Times

Placebos Prove So Powerful Even Experts Are Surprised

New Studies Explore the Brain's Triumph Over Reality

By SANDRA BLAKESLEE

Many doctors know the story of "Mr. Wright," who was found to have cancer and in 1957 was given only days to live. Hospitalized in Long Beach, Calif., with tumors the size of oranges, he heard that scientists had discovered a horse serum, Krebiozen, that appeared to be effective against cancer. He begged to receive it.

His physician, Dr. Philip West, finally agreed and gave Mr. Wright an injection on a Friday afternoon. The following Monday, the astonished doctor found his patient out of his "death bed," joking with the nurses. The tumors, the doctor wrote later, "had melted like snowballs on a hot stove."

Two months later, Mr. Wright read medical reports that the horse serum was a quack remedy. He suffered an immediate relapse. "Don't believe what you read in the papers," the doctor told Mr. Wright. Then he injected him with what he said was "a new super-refined double strength" version of the drug. Actually, it was water, but again, the tumor masses melted.

Mr. Wright was "the picture of health" for another two months — until he read a definitive report stating that Krebiozen was worthless. He died two days later.

Doctors who know this story dismiss it as one of those strange tales that medicine cannot explain. The idea that a patient's beliefs can make a fatal disease go away is too bizarre.

But now scientists, as they learn that the placebo effect is even more powerful than anyone had been able to demonstrate, are also beginning to discover the biological mechanisms that cause it to achieve results that border on the miraculous. Using new techniques of brain imagery, they are uncovering a host of biological mechanisms that can turn a thought, belief or desire into an agent of change in cells, tissues and organs. They are learning that much of human perception is based not on information flowing into the brain from the outside world but what the brain, based on previous experience, expects to happen next.

Placebos are "lies that heal," said Dr. Anne Harrington, a historian of science at Harvard University. A placebo, Latin for "I shall please," is typically a sham treatment that a doctor doles out merely to please or placate anxious or persistent patients, she said. It looks like an active drug but has no pharmacological properties of its own.

Until fairly recently, nearly all of medicine was based on placebo effects, because doctors had little effective medicine to offer. Through the 1940's, American doctors handed out sugar pills in various shapes and colors in a deliberate attempt to induce placebo responses.

Nowadays, doctors have real medicines to fight disease. But these treatments have not diminished the power of the placebo.

Doctors in Texas are conducting a study of arthroscopic knee surgery that uses general anesthesia in which patients with sore, worn knees are assigned to one of three operations — scraping out the knee joint, washing out the joint by doing nothing. In the "nothing" operation, doctors anesthetize the patient, make three little cuts in the knee as if to insert the usual instruments and

A Medical Mystery

Scientists have long been amazed by the way dummy drugs can have real effects. A new examination is helping them understand this placebo effect, a triumph of expectation over reality.

A Magic Act Evolves

The placebo effect may be related to an evolutionary advantage in acting first, analyzing later. Expectation can produce powerful physiological results as it does in the face-of-perceived danger.



1 OBSERVATION

A man walks through the forest and spies a long, thin brown object in the high grass.



2 INTERPRETATION

The lower brain processes sensory input: there is no sound or movement, the object has a dark exterior. It looks like a stick.



3 EXPECTATION Simultaneously, the upper brain, drawing on experience, interprets information from the senses and comes to a different conclusion: snake!

4 RESOLUTION The brain may give equal weight to input from the internal and external worlds. But if expectation wins out, the body will produce stress hormones in response to the stick.

Jim McManus/The New York Times

Doctors uncover mechanisms that can turn belief into an agent of biological change.

then pretend to operate. Two years after surgery, patients who underwent the sham surgery reported the same amount of relief from pain and swelling as those who had had the real operations.

A recent review of placebo-controlled studies of modern antidepressant drugs found that placebos and genuine drugs worked about as well. "If you expect to get better, you will," said Dr. Irving Kirsch, a psychiatrist at the University of Connecticut who carried out the review. His findings were met with a great deal of skepticism.

And a recent study of a baldness remedy found that 86 percent of men taking it either maintained or showed an increase in the amount of hair on their heads. But so did 42 percent of the men taking a placebo.

Some studies are specifically designed to explore the power of placebos rather than drugs. On Coche Island in Venezuela, asth-

The Body Heals Itself

New studies show the placebo effect at work from head to toe in different cultures around the world.

Hair Growth

Forty-two percent of balding men taking a placebo either maintained or increased the amount of hair on their heads.

Asthma

Smelling a placebo helped asthmatic children in Venezuela increase their lung function by 33%.

Allergies

In a Japanese study, people exposed to fake poison ivy developed real rashes.

Joint Repair

Doctors in Texas studying knee surgery found similar levels of pain relief whether surgery was real or feigned.

Pain

When told a heavy object was about to hit their foot, people in a study exhibited the kind of brain activity researchers associate with pain perception.

matic children were given a sniff of vanilla along with a squirt of medicine from a bronchodilator twice a day. Later, the vanilla odor alone increased their lung function, 33 percent as much as did the bronchodilator alone.

And at Tulane University, Dr. Eileen Palace is using a placebo to restore sexual arousal in women who say they are nonorgasmic. The women are hooked up to a biofeedback machine that they are told measures their vaginal blood flow, an index of arousal. Then they are shown sexual stimuli that would arouse most women. But the experimenter plays a trick on the women by sending, within 30 seconds, a false feedback signal that their vaginal blood flow has increased. Almost immediately they then become genuinely aroused.

Placebos are about 55 percent to 80 percent as effective as most active medications like aspirin and codeine for controlling pain, Dr. Kirsch said. Moreover, placebos that relieve pain can be blocked with a drug, naloxone, that also blocks morphine.

For a while, many scientists thought that placebos might work by releasing the body's natural morphine-like substances, called endorphins. But that is not the only explanation, he said. While placebos can act globally on the body, they can also have

The Power of the Placebo Amazes Medical Experts

Continued From First Science Page

extremely specific effects. For example, a study was carried out in Japan on 13 people who were extremely allergic to poison ivy. Each was rubbed on one arm with a harmless leaf but were told it was poison ivy and touched on the other arm with poison ivy and told it was harmless. All 13 broke out in rash where the harmless leaf contacted their skin. Only two reacted to the poison leaves.

Studies have shown, time and again, that placebos can work wonders. Like "real drugs," they can cause side effects like itching, diarrhea and nausea. They can lead to changes in pulse rate, blood pressure, electrical skin resistance, gastric function, penis engorgement and skin conditions. The question is, why? Explanations of why placebos work can be found in a new field of cognitive neuropsychology called expectancy theory — what the brain believes about the immediate future.

'We are misled by dualism or the idea that mind and body are separate.'

Like classical conditioning theory (Pavlov's dogs salivate at the sound of the bell), expectancy involves associative learning. The medical treatments you get during your life are conditioning trials, Dr. Kirsch said. The doctor's white coat, nurse's voice, smell of disinfectant or needle prick have acquired meaning through previous learning, producing an expectation of relief from symptoms. Each pill, capsule or injection is paired with active ingredients, and later, if you get a pill without active ingredients, you can still get a therapeutic effect, he said.

Such conditioning shows how expectations are acquired, Dr. Kirsch said. But it does not explain the strength and persistence of placebo effects. These responses occur almost instantly, with no apparent conscious thought, and are therefore wired firmly into the brain, he said.

Response expectations are strong because the world is filled with ambiguity. A long thin object seen in dim light could be a stick or a snake. But it may not be safe to take the time to find out. So people evolved a

mechanism to anticipate what is going to occur. This expectation speeds the perceptual processing at the expense of accuracy.

As in the outside world, people's internal states have inherent ambiguity. That is why, when people in an experiment were given a drug that produced a surge of adrenaline, they interpreted the feeling as anger, euphoria or nothing at all, depending on what they had been told to expect.

Critics of alternative medicine say its enduring appeal is explained by the placebo effect. When conventional therapies fail to help chronic or poorly understood conditions, the acupuncturist, homeopathist or chiropractor steps into the breach with a potent belief system ready-made to help the suffering patient. "If a guy in a white coat or a guy dressed in feathers can induce a patient's immune system to fight back, who is to say which is better?" said Dr. Dan Moleran, a medical anthropologist at the University of Michigan at Dearborn.

Support for the expectancy theory emerged about 10 years ago, when many scientists realized how closely the brain, the immune system and the hormone production of the endocrine system are linked. Chronic stress sets into motion a cascade of biological events involving scores of chemicals in the body — serotonin, cortisol, cytokines, interleukins, tumor necrosis factor and so on.

Such stress lowers resistance to disease and alters gene expression. When people are under stress, wounds tend to heal more slowly, latent viruses like herpes erupt and brain cells involved in memory formation die off. The precise molecular steps underlying all of these changes have been mapped out.

But what about the opposite? Can a thought or belief produce a chemical cascade that leads to healing and wellness? Researchers studying placebos think the answer is yes, and they offer several ways it might work:

¶A placebo might reduce stress, allowing the body to regain some natural, optimum level called health.

¶Special molecules may exist that help carry out placebo responses. For example, a recent study found that stressed animals can produce a valium-like substance in their brains, but only if they have some control over the source of the stress. People almost certainly have similar brain chemistry.

¶Placebos may draw their power from the way the brain is organized to act on what experience predicts will happen next.

Dr. Marcel Kinsbourne, a neuroscientist at the New School for Social Research in New York, explains it this way: The brain generates two kinds of activation patterns, which arise from networks of neurons firing

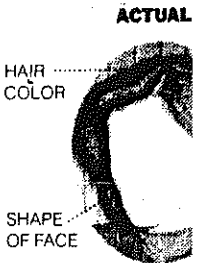
Expectancy Theory Fills in the

In addition to the medical miracles of placebos on expectancy affects many aspects of ordinal

EXAMPLE 1

Say, isn't that...

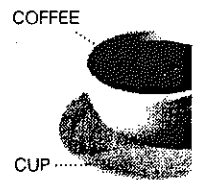
When seeing someone partially or from a distance, the brain fills in unclear or unseen elements, turning the stranger across the room into a familiar face.



EXAMPLE 2

Ah, a hot cup of Joe...

The sight of the first morning pick-me-up conjures expectations of warmth, flavor and the stimulating effects of caffeine regardless of actual content.



EXAMPLE 3

Hey, where's that step?

When the brain's expectation doesn't jibe with the reality, as when one expects an additional step on a staircase, a quick sense of surprise and confusion results.



together. One type is set in motion by information flowing into the brain from the outside world — smells, tastes, visual images, sounds. At the same time, the cortex draws on memories and feelings to generate patterns of brain activity related to what is expected to happen.

The top-down patterns generated by the cortex intersect smoothly with the bottom-up patterns to inform us about what is happening, Dr. Kinsbourne said. If there is a mismatch, the brain tries to sort it out, without necessarily designating one set of patterns as more authoritative than another.

The expectations that result are internally generated brain states that can be as real as anything resulting purely from the outside world. For example, recent experiments with monkeys show that if they expect a reward like a sip of apple juice, cells in their brains fire 20 to 30 seconds before they actually receive it. In other words, expectancies are embedded in the brain's neurochemistry.

"We are misled by dualism or the idea that mind and body are separate," said Dr. Howard Fields, a neuroscientist at the University of California at San Francisco who

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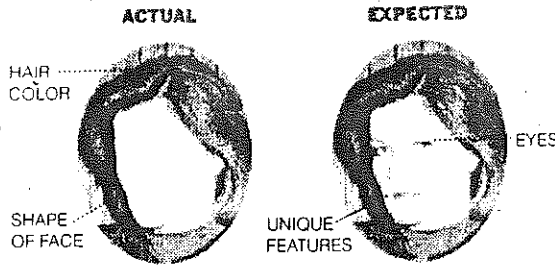
Expectancy Theory Fills In the Blanks

In addition to the medical miracles of placebos, the brain's reliance on expectancy affects many aspects of ordinary life.

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Say, Isn't that...

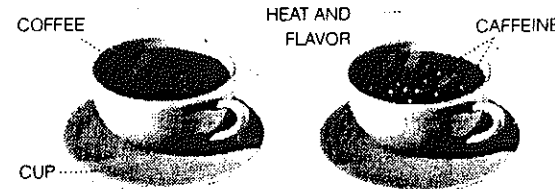
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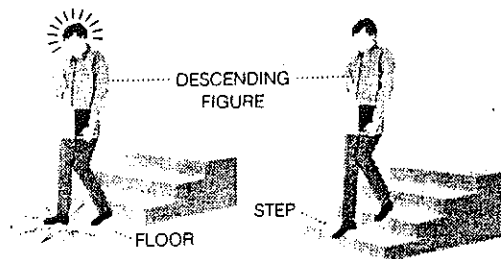
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The New York Times

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"We are misled by dualism or the idea that mind and body are separate," said Dr. Howard Fields, a neuroscientist at the University of California at San Francisco who

Examining the remarkable power of the placebo effect — lies that heal.

studies placebo effects. A thought is a set of neurons firing which, through complex brain wiring, can activate emotional centers, pain pathways, memories, the autonomic nervous system and other parts of the nervous system involved in producing physical sensations, he said.

Morphine will alter brain patterns to reduce pain. So will a placebo. Obviously, placebos have limits. Mr. Wright's miraculous remission aside, most people cannot think, hope or believe their way out of cancer or AIDS.

As Dr. Howard Spiro, a gastroenterologist at Yale University, put it: Some diseases are unleashed with the power of a firehose. Others unfold at a trickle, and perhaps those are the ones amenable to placebo effects.

Enthusiasm Of Doctor Can Give Pill Extra Kick

By SANDRA BLAKESLEE

Though some people respond more strongly to placebos than others do, it seems that everyone responds at some time or other. And doctors seem to play a large role in the degree of that response.

"The thing that trumps everything is the enthusiastic physician," said Dr. Dan Molerman of the University of Michigan. For example, one study offered the same drug to patients with identical symptoms, with one difference. Some were told by their physicians, "This drug has been shown to work," while others were told, "I am not sure if this treatment will work — let's just try it." The first group of patients did much better, Dr. Molerman said. "The physician is an agent for optimism and hope and a great inducer of beliefs."

Physicians can even fool themselves. Years ago, researchers carried out controlled studies of a drug for angina or heart pain and found it was no better than a placebo, Dr. Molerman said. Once doctors knew that, its effectiveness fell.

While doctors and patients affect one another's expectations, both are swept up into a wider context of culture and biology, said Dr. David Morris, an adjunct professor of medicine at the University of New Mexico in Albuquerque. The brain circuits through which placebos act, he said, are activated through the experience of living in a particular culture.

To explore the importance of cultural context, Dr. Molerman, in an analysis forthcoming in the journal *Medical Anthropology Quarterly*, compared 122 double-blind placebo-controlled ulcer studies from all over the world. Doctors used the same techniques, the same drugs and the same placebo pills and studied an image of the stomach lining before and after treatment to see what worked. The drugs worked 75 to 80 percent of the time, Dr. Molerman said, whereas the placebos worked from zero to 100 percent of the time, depending on the country. The placebo healing rate for ulcers in Germany was 60 percent, almost double the world average of 36 percent, which is about where the United States fell. But in Brazil, the mean placebo healing rate was a startling 6 percent.

"I don't have hint of what is going on here," Dr. Molerman said. "I can only say that cultural differences affect ulcer treatments, even though ulcers are the same the world over."